

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Currently Amended) A biocompatible gel-forming drug-delivering composition for *in vivo* administration, comprising:

a drug;

a first component comprising at least one sulfhydryl group-containing compound in a liquid medium having an alkaline pH, wherein said sulfhydryl group-containing compound is given by the formula  $\text{Core}_1\text{-(SH)}_m$ , wherein  $m \geq 2$ ; and

a second component comprising at least one sulfhydryl reactive group-containing compound in either a liquid medium having a neutral or acidic pH or in powder form, wherein said sulfhydryl reactive group-containing compound is given by the formula  $\text{Core}_2\text{-Y}_n$ , wherein Y is a sulfhydryl reactive group and wherein  $n \geq 2$ ;

wherein the biocompatible gel-forming drug-delivering composition further comprises a secondary carrier, the secondary carrier being polymeric microspheres that incorporate incorporating the drug, wherein the drug is hydrophobic; and wherein at least one of the first or second components is a polyalkylene oxide and wherein the sulfhydryl groups and the sulfhydryl reactive groups react with one another to form covalent bonds therebetween when said components are mixed together to form a gel in less than one minute.

2. (Original) The composition of claim 1, wherein m and n are each 4.

3. (Original) The composition of claim 1, wherein m and n are each 12.

4. (Original) The composition of claim 1, wherein the first component is a polyalkylene oxide.

5. (Original) The composition of claim 1, wherein the second component is a polyalkylene oxide.

6. (Original) The composition of claim 1, wherein the first and second components are polyalkylene oxides.

7. (Withdrawn) The composition of claim 6, wherein the polyalkylene oxides are polyethylene glycol.

8. (Withdrawn) The composition of claim 1, wherein only one of the first or second components is a polyalkylene oxide.

9. (Withdrawn) The composition of claim 8, wherein one of the components is a polyalkylene oxide and the other component is a functionally activated succinimidyl or maleimidyl compound which is not a polymer.

10. (Original) The composition of claim 1, wherein the covalent bonds are thioester linkages.

11. (Withdrawn) The composition of claim 1, wherein the covalent bonds are thioether linkages.

12. (Withdrawn) The composition of claim 1, wherein the covalent bonds are sulfhydryl linkages.

13. (Canceled)

14. (Original) The composition of claim 1, wherein the drug is an angiogenesis inhibitor.

15. (Withdrawn) The composition of claim 1, wherein the drug is a 5-Lipoxygenase inhibitor or antagonist.

16. (Withdrawn) The composition of claim 1, wherein the drug is a chemokine receptor antagonist.

17. (Original) The composition of claim 1, wherein the drug is a cell cycle inhibitor or an analogue or derivative thereof.

18. (Original) The composition of claim 17, wherein the cell cycle inhibitor is a microtubule stabilizing agent.

19. (Original) The composition of claim 18, wherein the microtubule stabilizing agent is paclitaxel, docetaxel, or Peloruside A.

20. (Original) The composition of claim 17, wherein the cell cycle inhibitor is a taxane.

21. (Original) The composition of claim 18, wherein the taxane is paclitaxel or an analogue or derivative thereof.

22. (Withdrawn) The composition of claim 17, wherein the cell cycle inhibitor is an antimetabolite, an alkylating agent, or a vinca alkaloid.

23. (Withdrawn) The composition of claim 22, wherein the vinca alkaloid is vinblastine, vincristine, vincristine sulfate, vindesine, vinorelbine, or an analogue or derivative thereof.

24. (Withdrawn) The composition of claim 17, wherein the cell cycle inhibitor is camptothecin or an analogue or derivative thereof.

25. (Withdrawn) The composition of claim 17, wherein the cell cycle inhibitor is selected from the group consisting of mitoxantrone, etoposide, 5-fluorouracil, doxorubicin, methotrexate, Mitomycin-C, CDK-2 inhibitors, and analogues and derivatives thereof.

26. (Withdrawn) The composition of claim 1, wherein the drug is a cyclin dependent protein kinase inhibitor or an analogue or derivative thereof.

27. (Withdrawn) The composition of claim 1, wherein the drug is an EGF (epidermal growth factor) kinase inhibitor or an analogue or derivative thereof.

28. (Withdrawn) The composition of claim 1, wherein the drug is an elastase inhibitor or an analogue or derivative thereof.

29. (Withdrawn) The composition of claim 1, wherein the drug is a factor Xa inhibitor or an analogue or derivative thereof.

30. (Withdrawn) The composition of claim 1, wherein the drug is a farnesyltransferase inhibitor or an analogue or derivative thereof.

31. (Withdrawn) The composition of claim 1, wherein the drug is a fibrinogen antagonist or an analogue or derivative thereof.

32. (Withdrawn) The composition of claim 1, wherein the drug is a guanylate cyclase stimulant or an analogue or derivative thereof.

33. (Withdrawn) The composition of claim 1, wherein the drug is a heat shock protein 90 antagonist or an analogue or derivative thereof.

34. (Withdrawn) The composition of claim 1, wherein the drug is an HMGCoA reductase inhibitor or an analogue or derivative thereof.

35. (Withdrawn) The composition of claim 1, wherein the drug is a hydroorotate dehydrogenase inhibitor or an analogue or derivative thereof.

36. (Withdrawn) The composition of claim 1, wherein the drug is an IKK2 inhibitor or an analogue or derivative thereof.

37. (Withdrawn) The composition of claim 1, wherein the drug is an IL-1, ICE, or IRAK antagonist or an analogue or derivative thereof.

38. (Withdrawn) The composition of claim 1, wherein the drug is an IL-4 agonist or an analogue or derivative thereof.

39. (Withdrawn) The composition of claim 1, wherein the drug is an immunomodulatory is rapamycin, tacrolimus, everolimus, biolimus, or an analogue or derivative thereof.

40. (Withdrawn) The composition of claim 1, wherein the drug is an inosine monophosphate dehydrogenase inhibitor or an analogue or derivative thereof.

41. (Withdrawn) The composition of claim 1, wherein the drug is a leukotrene inhibitor or an analogue or derivative thereof.

42. (Withdrawn) The composition of claim 1, wherein the drug is a MCP-1 antagonist or an analogue or derivative thereof.

43. (Withdrawn) The composition of claim 1, wherein the drug is a MMP inhibitor or an analogue or derivative thereof.

44. (Withdrawn) The composition of claim 1, wherein the drug is a NF kappa B inhibitor or an analogue or derivative thereof.

45. (Withdrawn) The composition of claim 1, wherein the drug is a NO antagonist or an analogue or derivative thereof.

46. (Withdrawn) The composition of claim 1, wherein the drug is a P38 MAP kinase inhibitor or an analogue or derivative thereof.

47. (Withdrawn) The composition of claim 1, wherein the drug is a phosphodiesterase inhibitor or an analogue or derivative thereof.

48. (Withdrawn) The composition of claim 1, wherein the drug is a TGF beta Inhibitor or an analogue or derivative thereof.

49. (Withdrawn) The composition of claim 1, wherein the drug is a thromboxane A2 antagonist or an analogue or derivative thereof.

50. (Withdrawn) The composition of claim 1, wherein the drug is a TNFa Antagonist, a TACE, or an analogue or derivative thereof.

51. (Withdrawn) The composition of claim 1, wherein the drug is a tyrosine kinase inhibitor or an analogue or derivative thereof.

52. (Withdrawn) The composition of claim 1, wherein the drug is a vitronectin inhibitor or an analogue or derivative thereof.

53. (Withdrawn) The composition of claim 1, wherein the drug is a fibroblast growth factor inhibitor or an analogue or derivative thereof.

54. (Withdrawn) The composition of claim 1, wherein the drug is a protein kinase inhibitor or an analogue or derivative thereof.

55. (Withdrawn) The composition of claim 1, wherein the drug is a PDGF receptor kinase inhibitor or an analogue or derivative thereof.

56. (Withdrawn) The composition of claim 1, wherein the drug is an endothelial growth factor receptor kinase inhibitor or an analogue or derivative thereof.

57. (Withdrawn) The composition of claim 1, wherein the drug is a retinoic acid receptor antagonist or an analogue or derivative thereof.

58. (Withdrawn) The composition of claim 1, wherein the drug is a platelet derived growth factor receptor kinase inhibitor or an analogue or derivative thereof.

59. (Withdrawn) The composition of claim 1, wherein the drug is a fibrinogen antagonist or an analogue or derivative thereof.

60. (Withdrawn) The composition of claim 1, wherein the drug is an antimycotic agent or an analogue or derivative thereof.

61. (Withdrawn) The composition of claim 1, wherein the drug is a bisphosphonate or an analogue or derivative thereof.

62. (Withdrawn) The composition of claim 1, wherein the drug is a phospholipase A1 inhibitor or an analogue or derivative thereof.

63. (Withdrawn) The composition of claim 1, wherein the drug is a histamine H1/H2/H3 receptor antagonist or an analogue or derivative thereof.

64. (Withdrawn) The composition of claim 1, wherein the drug is a macrolide antibiotic or an analogue or derivative thereof.

65. (Withdrawn) The composition of claim 1, wherein the drug is an GPIIb IIIa receptor antagonist or an analogue or derivative thereof.

66. (Withdrawn) The composition of claim 1, wherein the drug is an endothelin receptor antagonist or an analogue or derivative thereof.

67. (Withdrawn) The composition of claim 1, wherein the drug is a peroxisome proliferators-activated receptor agonist or an analogue or derivative thereof.

68. (Withdrawn) The composition of claim 1, wherein the drug is an estrogen receptor agent or an analogue or derivative thereof.

69. (Withdrawn) The composition of claim 1, wherein the drug is somatostatin or an analogue or derivative thereof.

70. (Withdrawn) The composition of claim 1, wherein the drug is a JNK Kinase inhibitor or an analogue or derivative thereof.

71. (Withdrawn) The composition of claim 1, wherein the drug is a melanocortin or an analogue or derivative thereof.



72. (Withdrawn) The composition of claim 1, wherein the drug is a raf kinase inhibitor or analogue or derivative thereof.

73. (Withdrawn) The composition of claim 1, wherein the drug is a lysylhydroxylase inhibitor or an analogue or derivative thereof.

74. (Withdrawn) The composition of claim 1, wherein the drug is an IKK 1/2 inhibitor or an analogue or derivative thereof.

75. (Original) The composition of claim 1, further comprising an anti-inflammatory agent, an antithrombotic agent, an antibiotic, or a combination thereof.

76-83. (Canceled)

84. (Currently Amended) The composition of claim 1, wherein the drug is a ~~hydrophobic drug~~ in admixture with the secondary carrier to provide a drug/secondary carrier combination, the drug/secondary carrier combination being further in admixture with the first component ~~to provide drug/carrier/first component, the drug/carrier/first component being suspended~~ in an aqueous buffer solution.

85-86. (Canceled)

87. (Original) The composition of claim 1, wherein the first component is suspended in a buffer solution comprising a mixture of phosphate buffer and carbonate buffer.

88. (Original) The composition of claim 2, wherein the second component comprises a mixture of succinimidyl polyalkylene oxide and maleimidyl polyalkylene oxide.

89. (Currently Amended) A method for treating tissues, comprising the steps of:

administering to a tissue site a first component comprising at least one sulfhydryl group-containing compound in liquid medium having an alkaline pH, wherein said sulfhydryl group-containing compound is given by the formula  $\text{Core}_1-(\text{SH})_m$ , wherein  $m \geq 2$ ; and

simultaneously or subsequently administering to the tissue site a second component comprising at least one sulfhydryl reactive group-containing compound either a liquid medium having a neutral or acidic pH or in powder form, wherein said sulfhydryl reactive group-containing compound is given by the formula  $\text{Core}_2-\text{Y}_n$ , wherein Y is a sulfhydryl reactive group and wherein  $n \geq 2$ , and wherein at least one of the first or second components is a polyalkylene oxide; and

simultaneously or subsequently administering to the tissue site a hydrophobic drug, the hydrophobic drug being ~~in admixture with a secondary carrier~~ incorporated in polymeric microspheres; and

allowing the sulfhydryl groups and the sulfhydryl reactive groups to react with one another to form covalent bonds therebetween to form a gel in less than one minute.

90. (Currently Amended) A biocompatible gel-forming drug-delivering composition for *in vivo* administration with a gel time of less than one minute, comprising:

polyalkylene oxide-(SH)<sub>4</sub> and a hydrophobic drug in a liquid medium having a pH of between 8 and 10.5, the hydrophobic drug being incorporated in ~~a secondary carrier~~ polymeric microspheres; and

polyalkylene oxide-Y<sub>4</sub>, wherein Y is succinimidyl, in a liquid medium having an acidic pH.

91. (Currently Amended) A biocompatible gel-forming drug-delivering composition for *in vivo* administration with a gel time of less than one minute, comprising:  
polyalkylene oxide-(SH)<sub>12</sub> and a hydrophobic drug in a liquid medium having an alkaline pH, the hydrophobic drug being incorporated in ~~a secondary carrier~~ polymeric microspheres; and  
polyalkylene oxide-Y<sub>12</sub> in a liquid medium having an acidic pH, wherein Y is a succinimidyl or maleimidyl group.

92. (Currently Amended) A biocompatible gel-forming composition for *in vivo* administration, comprising:  
a sulfhydryl group-containing polyalkylene oxide in a liquid medium having an acidic pH, wherein said sulfhydryl group-containing polyalkylene oxide is given by the formula Core-(SH)<sub>m</sub>, wherein  $m \geq 2$ ;  
a buffer solution with an alkaline pH; and  
a hydrophobic drug in admixture with the polyalkylene oxide and/or the buffer solution, wherein the hydrophobic drug is incorporated in ~~a secondary carrier~~ polymeric microspheres;  
wherein the sulfhydryl groups react with one another to form covalent bonds therebetween when said components are mixed together to form a gel in less than one minute.

93. (Currently Amended) A biocompatible gel-forming drug-delivering composition for *in vivo* administration, comprising:  
at least one sulfhydryl group-containing compound in a liquid medium having an alkaline pH, wherein said sulfhydryl group-containing compound is given by the formula Core<sub>1</sub> - (SH)<sub>m</sub>, wherein  $m \geq 2$ ;  
at least one sulfhydryl reactive group-containing compound either a liquid medium having a neutral or acidic pH or in powder form, wherein said sulfhydryl reactive group-containing compound is given by the formula Core<sub>2</sub> - Y<sub>n</sub>, wherein Y is a sulfhydryl reactive group and wherein  $n \geq 2$ ;

at least one hydrophobic drug in admixture with either or both of the at least one sulfhydryl group-containing compound and the at least one sulfhydryl reactive group-containing compound, the hydrophobic drug being incorporated in a secondary carrier, the secondary carrier comprising polymeric microspheres; and

collagen;

wherein at least one of either the sulfhydryl group-containing compound or the sulfhydryl reactive group-containing compound is a polyalkylene oxide, and wherein the sulfhydryl groups and the sulfhydryl reactive groups are capable of reacting with one another to form covalent bonds therebetween.

94. (Original) The composition of claim 93, wherein m and n are each 4.

95. (Original) The composition of claim 93, wherein m and n are each 12.

96. (Original) The composition of claim 93 wherein the sulfhydryl group-containing compound is a polyalkylene oxide.

97. (Original) The composition of claim 93, wherein the sulfhydryl reactive group-containing compound is a polyalkylene oxide.

98. (Original) The composition of claim 93, wherein both the sulfhydryl group-containing compound and the sulfhydryl reactive group-containing compound are polyalkylene oxides.

99. (Original) The composition of claim 98, wherein both the sulfhydryl group-containing compound and the sulfhydryl reactive group-containing compound are polyalkylene oxides.

100. (Withdrawn) The composition of claim 93, wherein only one of the first or second components is a polyalkylene oxide.

101. (Withdrawn) The composition of claim 100, wherein one of the components is a polyalkylene oxide and the other component is a functionally activated succinimidyl or maleimidyl compound which is not a polymer.

102. (Original) The composition of claim 93, wherein the covalent bonds are thioester linkages.

103. (Withdrawn) The composition of claim 93, wherein the covalent bonds are thioether linkages.

104. (Withdrawn) The composition of claim 93, wherein the covalent bonds are sulfhydryl linkages.

105. (Canceled)

106. (Currently Amended) The composition of claim 93, wherein the drug is a ~~hydrophobic drug~~ in admixture with a secondary carrier to provide a drug/secondary carrier combination, the drug/secondary carrier combination being further in admixture with either or both of the at least one sulfhydryl group-containing compound and the at least one sulfhydryl reactive group-containing compound.

107. (Original) The composition of claim 93, wherein the sulfhydryl group-containing compound is suspended in a buffer solution comprising a mixture of phosphate buffer and carbonate buffer.

108. (Original) The composition of claim 93, wherein the sulfhydryl reactive group-containing compound comprises a mixture of succinimidyl polyalkylene oxide and maleimidyl polyalkylene oxide.

109. (Original) The composition of claim 93, wherein the collagen is methylated collagen.

110. (Currently Amended) A biocompatible gel-forming drug-delivering composition for *in vivo* administration, comprising:

- (a) a first component in a liquid medium having an acidic pH comprising:
  - (i) at least one sulfhydryl group-containing compound given by the formula  $\text{Core}_1-(\text{SH})_m$ , wherein  $m \geq 2$ ;
  - (ii) at least one sulfhydryl reactive group-containing compound given by the formula  $\text{Core}_2-\text{Y}_n$ , wherein Y is a sulfhydryl reactive group and wherein  $n \geq 2$ ; and
  - (iii) collagen; and
- (b) a second component comprising a buffer having a pH of between 8 and 10.5;

wherein a hydrophobic drug is present in admixture with either or both of the first component or the second component, the hydrophobic drug being further incorporated in a secondary carrier polymeric microspheres; and

wherein at least one of either the sulfhydryl group containing compound or the sulfhydryl reactive group containing compound is a polyalkylene oxide.

111. (Original) The composition of claim 110 wherein the collagen is methylated collagen.

112. (Original) The composition of claim 110 wherein the second component is a buffer solution comprising a mixture of phosphate buffer and carbonate buffer.

113-126. (Canceled)

127. (New) The composition of claim 1 wherein the polymeric microspheres are formed of a polymer or copolymer comprising one or more monomers selected from the group consisting of lactic acid, glycolic acid, D-lactide, L-lactide, D,L-lactide, glycolide,  $\epsilon$ -caprolactone, trimethylene carbonate, 1,4-dioxane-2-one and 1,5-dioxepan-2-one.

128. (New) The composition of claim 127 wherein the copolymer is a block copolymer represented by A-B, A-B-A or B-A-B, wherein A is a poly(alkylene oxide) and B is a degradable polyester.

129. (New) The composition of claim 128 wherein A is poly(ethylene glycol), poly(propylene glycol), copolymers of ethylene oxide and propylene oxide or mono alkyl ethers thereof.